Guide to the Screen Version of the Carcinogenic Potency Database

This guide to the screen version of the CPDB plot is intended to facilitate use of the data. The same results are reported as in the 2-sided published plots.

The plot includes results of 6153 experiments on 1485 chemicals, and is organized alphabetically by chemical name. The plotted logarithmic scale of TD_{50}s included in the published plot format is not included here. Experiments are listed under the name of the test agent, and each experiment is identified by a unique number in the plot. This format is amenable to both Web viewing and printing. The plot is searchable by chemical name, CAS number, or author.

Below is an example from the plot of one experiment on phenolphthalein from the NCI/NTP bioassays, which will be used to describe variables included in the plot, the codes and conventions, and the Appendices. At the top of the example is a header describing the type of information in each field. The header should be read across, alternating between the top and bottom line: first "Spe" then "Sex" then "Strain" etc. The data is presented in 3 sections: 1) chemical information (red), 2) for each experiment on that chemical, a single line containing information on experimental protocol (blue), and 3) several lines of information on tumor incidence, potency, statistical significance and dose response for each tissue tumor combination reported (black). An experiment is defined as one sex of one species using a given route of exposure from one research report. The codes in the CPDB are mnemonic for ease of use. Throughout this guide the term "the plot" refers to this screen version.

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Chemical  Synonym   CAS number
[1]           [2]   [3]
PHENOLPHTHALEIN   77-09-8

   Spe  Strain    Xpo+Xpt  Details                                                                  Literature Reference
     Sex    Route      RefNum                  0 Dose  1 Dose   2 Dose  3 Dose
[4] [5][6][7] [8]   [9]  [10] [11]                      [12]    [13]    [14]                                  [15]
4661 M f b6c eat 24m24 TR465 :                    0    388.mg  777.mg  1.55gm                               NCI/NTP

 Site      Notes        DR       AuOp        UpConf                                                                Brkly Code
    Hist         TD50    2Tailpvl    LoConf        Cntrl   1 Inc    2 Inc   3 Inc          Pathology
[16] [17]   [18]  [19] [20] [21] [22] [23]   [24]     [25]    [26]     [27]    [28]     [29]                  [30]
 MXB MXB         508.mg Z P<.0005    296.mg 1.53gm  15/50   33/50    40/50   (36/50)  ---:hcs,lmt,mly; ova:sxb,sxs. C
 --- mly         748.mg Z P<.003  c  394.mg 4.88gm  15/50   28/50    33/50   (25/50)
 --- lmt         1.61gm Z P<.003  c  859.mg 8.28gm   1/50    9/50    10/50    (7/50)
 ova MXA         1.90gm Z P<.003  c  1.00gm 8.68gm   0/50    7/50     6/50    (5/50)   ova:sxb,sxs.
 --- hcs         4.08gm * P<.0005 c  2.27gm 11.7gm   0/50    2/50     7/50     7/50
 TBA MXB         1.74gm * P<.2       642.mg n.s.s.  40/50   39/50    47/50   43/50
 liv MXB         no dre   P=1.       3.96gm n.s.s.  21/50    3/50     6/50    (2/50)   liv:hpa,hpb,hpc.
 lun MXB         9.19gm * P<.3       2.56gm n.s.s.   6/50    5/50     6/50     8/50    lun:a/a,a/c.
```

Using this example, we give details of the information in each field identified with a set of numbers **[1] - [30]**; this set of numbers is for illustrative purposes only and does not appear in the plot. In the phenolphthalein example, the first line (columns **[1] - [3]**) provides chemical information, the second line (columns **[4] - [15]**) provides experimental protocol information with reference to the original paper, and subsequent lines (columns **[16] - [30]**) provide information on experimental results for each tissue-tumor combination.

Chemical information (red color)

[1], [2] The *chemical name* in capitals is indicated under **[1]** in the top line for a set of experiments. In the plot, common synonyms follow the name under **[2]**. In the example, phenolphthalein has no synonym.

[3] The *Chemical Abstracts Service Registry Number* (CAS #); in the example, 77-09-8.

Experimental protocol information (blue color)

[4] Under **[4]** is the unique plot number for each experiment, i.e., one sex of one species from one research report. In the phenolphthalein example, we use the line number 4661 which corresponds to the number in the plot. Each consecutive number in the plot indicates a separate experiment.

[5] The *species* used in the example is indicated under **[5]** as "M". The letter "M" refers to mice, "R" to rats, "H" to hamsters, "D" to dogs, "N" to prosimians, and "P" to monkeys.

[6] The *sex* is indicated by "f" for female (as in the phenolphthalein example), "m" for male under **[6]**. Occasionally an author in the literature will report data only for both sexes together, and in these cases the code used is "b" for both.

[7] The *strain or stock* of animal is reported as a three-letter-code under strain **[7]**. In the example, the mouse strain is indicated by b6c for $B6C3F_1$. Strain codes and definitions are listed in the Strain Appendix. Strains are coded just as they are referred to in the original publication. No attempt has been made to standardize the strain names; therefore, if different nomenclature is used by two authors who actually tested the same strain, then two different codes are used in the database. For monkeys and prosimians, this column is used for the species code, e.g., "rhe" for rhesus.

[8] The *route of administration* is indicated in the header line by "Route" and reported as a three-letter-code under **[8]**. In the phenolphthalein example, "eat" stands for administration in the diet. Route codes are listed in the Route Appendix and use mnemonic codes like "gav" for gavage.

[9] The *exposure and experiment time* are indicated under **[9]**. Exposure time is the period over which the test agent is administered; if administration was 5 times a week for 40 weeks, for example, the exposure time is 40 weeks. Experiment time is the total time on test; it is not the age of the animals. It is measured from the start of the experiment to the time of death of the last dosed animal. Within a single experiment, all tissue-tumor combinations have the same exposure time and the same experiment time. Both times are always reported in the same units. When both are less than 100 weeks, exposure and experiment time are reported as "w" for weeks; when greater than this, "m" for months is used. For tests in long-lived experimental animals like dogs and nonhuman primates, "y" for years may also be used. When exposure time and experiment time are equal, then the duration of dosing was for the entire experiment. In the example, the mice were dosed for 24 months, and the experiment ended at 24 months. Additional information about dosage in the units administered, the pattern of dosing, and survival for each experiment is reported in the supplementary dataset (http://potency.berkeley.edu/CPDBsupplementary-tab.html).

[10] The unique *reference number* assigned to each paper in the database. For NCI/NTP bioassays, this is the Technical Report number, TR465 in the example. For literature tests this is a unique paper identification number assigned to each paper.

[11] When the TD_{50} has been calculated using lifetable data, a ":" appears in column **[11]** (as in the example), otherwise it is blank. For a few experiments, the test did not meet our standard criteria. For these cases, a "()" appears in column **[11]**. The length criteria have been relaxed for studies in nonhuman primates (see Species Appendix). The exposure or experiment length usually was a week shorter than the inclusion rule, and the study was positive. For some early NCI experiments pooled controls were used in evaluating evidence for carcinogenicity in the Technical Report, and we have calculated TD_{50}s with those pools as well as the matched controls. Data using pooled controls are indicated by the word "pool" under column **[11]**, and by assigning a different experiment number to the pooled data. In some recent NTP bioassays, results for the kidney were reported in the Technical Reports for the standard histopathology protocol and separately for results including additional sections of the kidney. In such cases the word "with step" appears under column **[11]**, for

the results that include the additional kidney sections; these are considered a separate experiment and get a new line number.

[12] – [14] Beginning in **[12]** we report the *average daily dose rate* (green color) in mg/kg body wt for the length of the experiment as calculated by us for each dose group in the experiment. For brevity we have used "mg" instead of "mg/kg bd wt/d" throughout the plot. In the example, there are three dose levels 388 mg/kg, 777 mg/kg, and 1.55 gm/kg. A description of the method for estimating the average daily dose level is at http://potency.berkeley.edu/text/methods.html.

[15] For the published literature, a citation is provided, listing the first author, code for the journal or book title, volume number, pages, and year of publication. The full titles of the four-letter-codes for the names of references are listed in the Journal Appendix. The abbreviation *pers.comm.* indicates that additional data were obtained through personal communication with the author. On the plot a new citation for a published paper is listed whenever experimental results are from a different paper, i.e. if several experiments are reported consecutively in the CPDB from a single paper, then the citation will not repeat. When the next experiments are from a different paper, the new citation will be reported. If additional experiments are later reported from an earlier citation, the citation will be repeated. If pathology codes appear under **[29]** as in the phenolphthalein example, results are for an NCI/NTP bioassay.

A bibliography of all papers is given in the literature and NCI/NTP appendices. The Literature Appendix gives complete citations to articles, books, and reports in the general literature. The NCI/NTP Appendix lists the NCI/NTP Technical Reports by chemical name, and indicates Technical Report number and year of publication.

Experimental results

[16] – [17] The *site and histopathology* are reported on this line under **[16]** and **[17]**, and are marked in the header line by "Site" and "Hist". Each is indicated by a three-letter-code, and the respective codes and definitions are provided in the tissue and tumor appendices. Three-letter-codes have been created so that they are similar to the words they represent; for example, the line reports "--- mly" which stands for "all sites, malignant lymphoma".

For the NCI/NTP bioassays and the general literature, the nomenclature reflects the terminology used in the Technical Report or the published paper. The operational rule has been to retain what is published and not reinterpret or rename diagnostic categories. Thus, when various authors use different nomenclature for the same tissue or morphologic type of tumor, two different codes are used in the database. Occasionally it has been necessary to replace an adjective used for a tissue with a noun, e.g., the database uses kidney when renal is used in a paper. Some special considerations about the reporting of site and histopathology information from each source of data are as follows:

NCI/NTP Bioassays

In the phenolphthalein example above, certain tissue and tumor codes are given in capital letters; these denote particular mixes of sites or tumor types from the NCI/NTP bioassays. (Capital letters are not used for papers in the published literature.) When these capitals appear, additional information about the specific pathology is presented under column **[29]**. These special capitalized codes are used in the plot for TD_{50}s based on special mixes of tissue and tumor types from the NCI/NTP bioassays:

The mandatory sites are denoted by "MXB" (for "Mix Berkeley") to indicate that the site was created especially for the CPDB and is not based upon the NCI/NTP evaluations in the Technical Reports. For every NCI/NTP experiment, the same mandatory sites are given per species: for mice, "liv

MXB" (liver mandatory), "lun MXB" (lung mandatory) and "TBA MXB" (all tumor-bearing animals); for rats, "liv MXB" and "TBA MXB".

As in the phenolphthalein example, the NCI/NTP mandatory sites are always listed last for the experiment, in the order TBA, liv, and lun. The specific pathology is given for liv MXB and lun MXB under column **[29]**.

"MXA" (for "Mix Author") is used to denote a combination of sites or tumor types which is taken directly from the Technical Report tables of primary tumors, and denotes a mix of tissues or tumors created in those tables. In the example, the site and histopathology for "ova MXA" are listed under **[29]**. Whenever MXA appears under column **[17]**, the sites and/or histopathology which were combined are listed under column **[29]**.

"MXB MXB" denotes that a combination of tissues and tumors has been created by our group (MXB for "Mix Berkeley"), which consists of the aggregates of sites and histopathology evaluated in the Technical Report as "carcinogenic" or "clear" or "some" evidence of carcinogenic activity. See the Berkeley Code Appendix. When "MXB" appears under columns **[16]** and **[17]** a Berkeley Code will be listed under column **[30]**.

Bioassays in the Published Literature

The site and pathology information from the literature experiments is given in the plot for individual tissues and tumors just as it is for the NCI/NTP bioassays. It is usually not possible to combine sites from the published literature because, unlike the data available from the NCI/NTP bioassays, information is seldom reported about multiple tumor incidence in the same animal. When an author does give information about aggregated tissue or tumor types, the code "mix" is used in the plot to denote that specific sites and tumors are described in the paper. When the tumor types are not specified, the code "tum" is used. Mandatory sites from experiments in the literature are included in the database for the same tissues as the NCI/NTP bioassays. A TD_{50} is calculated for any mix of tumors reported in the mandatory site and for individual tumor types as well. All codes are in lower case letters.

[18] *Notes* under column **[18]**, provide additional information about the experiment in single-letter-codes which are defined in the Notecodes Appendix. This information is helpful in evaluating the experimental data. In the phenolphthalein example, there are no notecodes. Notecodes indicate such factors as: survival problems (notecode "s"), variable dosing protocol (notecode "v"), serial sacrifice as part of a longer study (notecode "k"), or that histopathological examination or reporting of results was restricted to only a few tissues (notecode "r"). In some recent NTP bioassays, results for the kidney are reported in the Technical Reports for the standard histopathology protocol and separately for results including additional sections of the kidney. In such cases the word "with step" appears under **[11]**, and a new line number appears in the plot for these results. Occasionally, when there is a "c", "p", "a", or "e" in the opinion column for an NCI/NTP bioassay, or a "+" for a test from the general literature, the positive evaluation was made because the incidence among dosed animals was high in comparison to historical control incidences; this occurs, for example, when there is a rare tumor among dosed animals. The actual numbers of animals bearing such tumors may be quite low, thus making the estimate of TD_{50} unreliable. In such cases, we have indicated that the author's opinion was based on historical control comparisons by putting an "h" notecode under column **[18]**.

The "most potent site" is determined by ordering the TD_{50}s in each experiment by statistical significance. If any TD_{50}s are significant at the $p<0.01$ level, then these are listed first, in order of potency. Then follow all TD_{50}s with $p<0.10$ sorted in order of potency. Last, all other TD_{50}s are listed in order of potency. For literature experiments, we have excluded the category "tba" from this sorting of the target sites, and have listed it last. For the NCI/NTP bioassays, the mandatory sites are excluded

from this sorted order, and are listed at the end in the order TBA MXB, liv MXB, and lun MXB (as in the phenolphthalein example).

In the example of phenolphthalein, there are five TD_{50}s with statistical significance $p<0.01$. The TD_{50} for "MXB MXB" is the most potent and thus appears first under column **[19]**. The estimated TD_{50} for "--- mly", appears next and has the opinion clear evidence of carcinogenic activity in the Technical Report (column **[22]**). These results indicate that 748 mg/kg body wt/day is estimated to halve the proportion of tumorless survivors at the end of a standard lifespan for female mice (in the absence of all other causes of death).

[19] The *value of each* TD_{50} is presented under column **[19]**, and includes the appropriate units (per kg) of body weight per day. The symbol "noTD50" appears instead of a numerical value whenever 100% of the dosed animals had the tumor(s) of interest and the TD_{50} was calculated with summary data. The symbol "no dre", for *no dose-related effect*, indicates that TD_{50} is not estimable for some other reason. For statistically non-significant TD_{50}s the numerical value may be impossibly large.

[20] The *shape of the dose-response curve* for each TD_{50} appears in **[20]** under the header "DR". The codes and definitions are listed in the Dose-response Curve Appendix. The shape of the dose-response has been determined by a test for departure from linearity. (See the Statistical Methods for Estimating TD_{50} Appendix.) If there was no significant departure from a linear dose-response, then the curve shape is listed as linear, and the symbol "*" appears. For experiments with three groups of animals including controls, a significant departure from linearity with upward curvature is denoted by the symbol "/". If there was a significant departure from linearity with downward curvature, then the TD_{50} is calculated without the data from the highest dose group, and the symbol "\" appears. We have adopted this convention to obtain the best estimate of TD_{50} by using only the linear portion of the dose-response curve in the calculation. The groups that are excluded from the reported TD_{50} calculation are indicated by parentheses around the tumor incidence data under **[27]** and **[28]**.

When there are more than three dose groups (including controls) in the TD_{50} calculation and there is a significant departure from linearity, the symbol "Z" is listed under **[20]**. When there is a blank space for the shape of the dose-response, there are two possible reasons. First, there may be only one dose group and a control group in the experiment, in which case there is not enough information to determine a curve shape. Second, there may be no dose-related effect, in which case the code "no dre" appears in **[19]** and "P=1." appears in **[21]**.

[21] The *two-tailed p-value* appears in **[21]**, under the header "2Tailpvl". This value indicates the statistical significance associated with testing whether the slope of the dose-response curve is different from zero. All values are given to one significant figure. When there is no dose-related effect or the slope is negative, then "P=1." appears in **[21]**. The lowest *p*-value reported is $p<0.0005$.

[22] The *opinion of the original author*, as to the tumorigenicity of the test agent at the site reported, is given under column **[22]**. Our rule for opinions from all sources of data has been to record all clearly stated evaluations of tumorigenicity at the site. (See the Author's Opinion Appendix.)

Some special considerations about our codes for author's opinion are as follows:

NCI/NTP Bioassays

Our conventions for reporting the author's opinions from the NCI/NTP Technical Reports are based upon the text of the Report and the statistical analysis tables. An author's opinion is listed for all sites except: Berkeley Mixes (MXB) and the statistical sites, i.e., those included in the tables but not considered evidence for carcinogenicity in the text of the Technical Report. For these cases, the opinion column is blank, as in the phenolphthalein example.

A "c" in the author's opinion column for NCI Technical Reports indicates that the text of the Report stated that at the site on which TD_{50} is based, the compound was *carcinogenic* under the conditions of the bioassay. For NTP Technical Reports, the Abstract indicated that there was "clear evidence of carcinogenic activity." See for example, the opinion column in the example of phenolphthalein for "--- mly", "--- lmt", "ova MXA" and "--- hcs". In NCI Technical Reports an "a" indicates an opinion that the incidence of tumors at that site(s) was evaluated as *associated* with administration of the compound under the conditions of the bioassay, or that the evidence for carcinogenicity was suggestive; these opinion codes in the CPDB are consistent with updated evaluations by NTP (Haseman *et al., Environ. Health Perspect.* 74: 229-235, 1987). For all NTP Technical Reports that use the current evaluation methodology, we report all sites listed in the summary table in the Abstract with the opinion for carcinogenic activity: "c" for clear, "p" for some, and "e" for equivocal (See Author's Opinion Appendix). The "a" opinion for NCI generally corresponds to an opinion of "e" for NTP.

The symbol "–" will appear in the opinion column for the most potent site in an NCI/NTP bioassay to denote the evaluation that the compound was not carcinogenic in that sex of that species under the conditions of the bioassay. In most cases, the "–" appears for the TD_{50} calculated for TBA, which is our convention whenever there is no evidence for carcinogenicity. For experiments evaluated as inadequate in the Technical Report, there is an "i" in the opinion column for the most potent site.

There are some cases when the "–" appears for a statistical site, i.e., one not evaluated as evidence for carcinogenicity in the Report, but which was statistically significant according to the statistical tables in the Report, and also had a TD_{50} significance level of $p<0.05$. When this site is the only evidence for a treatment-related effect, and thus the most potent site, we have indicated this by placing a "–" in the opinion column and flagging the TD_{50} with a # sign in column **[18]**.

For bioassays in which some target sites were evaluated as treatment-related, the statistical sites are also reported but the opinion column is left blank. In order to make it clear that NCI/NTP did not evaluate these statistical sites as evidence of carcinogenicity, we put an "S" for *statistical* in column **[30]**.

Bioassays in the Published Literature

In the general literature whenever the author evaluated the proportion of animals with tumors at a particular site as treatment-related, a "+" will appear in the opinion column **[22]** for that site. Such stated opinions as "positive," "carcinogenic," "induced," "treatment-related," and "tumorigenic," fit this category. The symbol "+" will only appear in the opinion column for a site in one of the following two cases: (1) the author gave a positive opinion for the particular target sites included in the TD_{50}, or (2) the occasional case where an author evaluated the compound as carcinogenic without specifying the target site, and we have indicated this with a "+" symbol in the opinion column for the category "all tumor bearing animals (tba)".

Similarly, the opinion column will contain a "–" only when either (1) the author stated an opinion that there was no carcinogenic effect at the particular sites included in the TD_{50}, or (2) the author concluded that there was no treatment-related effect in the experiment, in which case all sites reported for the experiment have a "–" in the opinion column.

Sites which an author did not evaluate as positive are included in the database only when the statistical significance associated with an increased percentage of dosed animals with tumors is $p<0.05$ (standard chi-square, one-sided p-value), or when the tissue is a mandatory site.

When no opinion about carcinogenicity is stated in the published paper for sites which are reported in the plot, the author's opinion column is left blank. This may occur either for mandatory sites, or for included sites which were not unequivocally evaluated by the author. If additional information

about evaluations was obtained directly from the author, then "pers.comm." appears after the citation under column **[15]**.

In summary, the symbol for the author's opinion column in the general literature reflects what the author actually stated in the paper or we were able to determine through personal communication. Sites evaluated as positive are given a "+". Sites evaluated as negative are given a "–". The symbol "+" is used for tba when the compound was evaluated as positive, and no specific target site was evaluated as positive. For all other opinions the author's opinion column is blank.

[23], [24] The *lower and upper confidence limits* for each TD_{50} are presented in **[23]** and **[24]** respectively. When the abbreviation "n.s.s." appears for either the lower or upper confidence limit, it denotes *not statistically significant.* Whenever the statistical significance of TD_{50} is $p>0.01$, then the upper 99% confidence limit will not be calculated. When the lower confidence limit is "n.s.s." this usually indicates that there were no tumors or only one tumor of the specified type in the experiment, and the lower confidence limit was not estimable; most often this occurs for mandatory sites. Occasionally the n.s.s. occurs for the lower confidence limit because 100% of dosed animals had the tumor(s) of interest and hence no lower confidence limit could be estimated with summary data.

[25] – **[28]** Beginning in **[25]** and extending through **[28]**, we report the *proportion of animals with tumors*. Column **[25]** is for the control group and columns **[26]** – **[28]** correspond to dose groups rates in columns **[12] – [14]**. The proportion of animals with tumors for TD_{50}s which have been calculated with lifetable data i.e. NCI/NTP studies, are presented here in summary form. The denominator reflects the starting number in each group.

Whenever the TD_{50} was calculated without the data from the highest dose group(s) (i.e., there was a significant downward departure from linearity), we have indicated this fact with parentheses around the incidences which were omitted from the final calculation. (See the Statistical Methods for Estimating TD_{50} Appendix.) Thus, whenever the shape of the dose-response is "\" under column **[20]** there are parentheses around the appropriate incidence data. Whenever there were more than three groups (including controls), and the dose-response was nonlinear, there is a "Z" under **[20]**. If the departure from linearity in such cases was downward, then this fact is indicated by parentheses around the tumor incidence for the group(s) that was excluded from the TD_{50} calculation. If there are no parentheses and a "Z" appears in the curve-shape column, then the dose-response had at least 3 doses and a control and curved upward. In the phenolphthalein example, --- mly has a "Z" under **[20]**, and the highest dose group is omitted from the final calculation of TD_{50}, as shown by parentheses around the tumor incidence in column **[28]**.

NCI/NTP Bioassays

For the proportion of animals with tumors, the number of animals reported in each group is the number at the *start* of the experiment; the TD_{50} was estimated with lifetable data. In the example, there were 50 in each group. For some early NCI experiments pooled controls were used in evaluating evidence for carcinogenicity in the Technical Report, and we have calculated TD_{50}s with those pools as well as the matched controls. Data using the pooled controls are indicated by the word "pool" under column **[11]**, and by reporting the pooled results as a separate experiment with a different line number.

Bioassays in the Published Literature

The proportion of animals with tumors presented is the number of animals used in the TD_{50} calculation. Many authors have reported only the starting number of animals. Whenever the published paper had additional information, i.e., the number of animals alive at the time of appearance of the first

tumor, or if that was not reported the number examined histologically at the site, then this number is used in the denominator of the proportion of animals with tumor. This is a more accurate description of the number of animals at risk of tumor. These data were used in the TD_{50} calculation and are reflected in columns **[25]** – **[28]**. In these cases, the notecode "e" for *effective number* appears in column **[18]**. Otherwise, the data reflect the number of animals started in each group. Since experimental designs vary in the literature, the incidence and dose-rate data may include a control and only one dose group or perhaps, a control and several dose groups. We correspond with about half the researchers about their published papers and are sometimes able to report tumor incidence data that is not given in the publication but improves the estimate of TD_{50}, e.g., number of animals alive at the first tumor in the denominator.

Whenever vehicle control data were available, either in NCI/NTP or general literature, these were used in the CPDB.

[29] For the NCI/NTP bioassays, we present the three-letter-codes for all *sites and histopathology* which are "Author's Mix" (MXA) or "Berkeley Mix" (MXB). This includes the MXB mandatory liver and lung sites, our combinations of sites which were individually evaluated as positive in the Report (MXB), the "statistical sites", and any combination of sites evaluated as treatment-related in the Technical Report (MXA). The three-letter-code for each tissue in the TD_{50} calculation is reported, and a ":" separates the tissues and tumors for each category of neoplasm included in the calculation. A "." follows the last three letter tumor code in each mix. The definitions for these codes are given in the tissue and tumor appendices.

[30] The last column of the plot, is used only for NCI/NTP bioassays. Under the header "Brkly Code", we indicate that a TD_{50} has been included in the database because of a decision rule of the Carcinogenic Potency Project (Berkeley) rather than because the sites were evaluated as treatment-related or combined in the NCI/NTP Technical Report. (See the Berkeley Codes Appendix.)

The capital letters "C", "M" and "P" are used in the Berkeley Code column for Berkeley Mixes (MXB). The letter "C" denotes a TD_{50} calculated for the combination of all sites evaluated in the Technical Report as clear evidence for *carcinogenicity* in this experiment. Line 4661 in the phenolphthalein example has a "C" under **[30]** because it is a combination of all animals having any tumor with a "C" opinion in **[22]**. The histopathology is listed under **[29]**, i.e. ---: hcs, lmt, mly; ova: sxb, sxs. The letter "P" denotes a combination of tumors evaluated as *some* evidence. The letter "M", for *mix,* is uncommon and denotes a combination of all sites evaluated as "C" or "P" in a bioassay where "clear" and "some" evidence were evaluations for different target sites in the same experiment. The letter "S" in column **[30]** is not a MXB, but rather indicates that the TD_{50} has been included in the plot because the sites were *statistically* significant in the tables of the Technical Report and the TD_{50} was significant at the $p<0.05$ level; however, NCI/NTP did not evaluate the site as evidence of carcinogenicity in the Technical Report. For all mandatory sites, the column for "Brkly Code" is blank.

In the plot, all bioassays of a particular chemical are organized under the chemical name, and these names are ordered alphabetically. Within each compound, the experiments are ordered alphabetically by species code, so that dogs would appear first, then hamsters, mice, prosimians, monkeys, and finally rats. Within a species, the bioassays are ordered by the code for the strain or stock. If there is an NCI/NTP bioassay of the chemical, then all experiments using that strain are reported first, followed by the strain used in any other experiments providing lifetable data, and finally by any remaining strains ordered alphabetically. Within the strain, the bioassays of females are reported first. Thus, when there is an NCI/NTP bioassay, "b6c" mice will appear first, and all experiments using "b6c" female mice would be reported before any experiments using "b6c" males.

To facilitate easy reference back to this guide when using the condensed plot, we have described each variable here in the order in which it appears in the plot. The titles in the header of the large plot also refer back to the categories in this guide. Abbreviations and symbols are defined in detail in the Appendices.